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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,782	09/08/2003	Phillip Arcangel	PP-19199.002	7355

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Intellectual Property - R440
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EXAMINER	
MCGAW, MICHAEL M	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,782	ARCANGEL ET AL.	
	Examiner	Art Unit	
	Michael M. McGaw	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 Nov 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,6-16,19 and 22-34* is/are pending in the application.

4a) Of the above claim(s) *33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,7-14,19 and 21-30* is/are rejected.

7)☒ Claim(s) *6, 15, 16, 22, 31, 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignment*.

DETAILED ACTION

Claims 1-32 were pending in the prior Office Action mailed August 13, 2004. Applicant has cancelled claims 1, 2, 4, 5, 17, 18, 20 and 21 in Applicant's response received November 18, 2004. Applicant has amended claims 3, 6, 15, 16, 19, 22, 31 and 32. Applicant has added claims 33 and 34. Claims 3, 6-16, 19 and 22-34 are currently pending.

Election/Restrictions

Newly submitted claims 33 and 34 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 33 and 34 depend upon previously rejected claims 3 and 19. Claims 3 and 19 were rejected in the previous Office Action under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (1999) in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. Claims 3 and 19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (1999) in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. and Choo, Q.L. et al. (1991). Claims 33 and 34 do not include all the limitations of previously searched subject matter deemed allowable and thus are beyond the scope of that which was previously searched.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 33 and 34 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112, ¶2

The rejection of claims 1, 2, 3 and 6 under 35 U.S.C. 112, 2nd paragraph is **withdrawn** pursuant to Applicant's amendments and explanations.

Applicant has removed the use of the term "first region" from the claims, rendering this rejection moot. Applicant has redefined the term "epitope" in the specification and more fully explained the their definition. Applicant has amended the claims to resolve the issue of an incompatible combination of closed language in the dependent claim followed by open claim language directed to the same term in dependent claims therefrom. Applicant has amended claims 6, 15, 16, 22, 31, and 32, thereby clarifying them, by removing references to figures, with sequence identification numbers in parentheses, and referred solely to the sequence identification number. Applicant has addressed the issues raised as to claims 9 and 25 by pointing to the fact that the underlying sequence includes a combination of previously defined epitopes, thus evidencing the operability of the epitopes.

Claim Rejections - 35 USC § 103

1. Claims 1-5, 7-14, 17-21, 23-25 and 26-30 were rejected in the previous Office Action under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (1999) in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. Claims 1, 2, 4, 5, 17, 18, 20 and 21 were cancelled rendering moot their rejection. Claims 3 and 19 have been amended to obviate the prior rejection. Thus, the prior rejection of claims 3, 7-8, 10-14, 19, 23-24

and 26-30 over Chien et al. (1999) in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. is withdrawn.

2. Claims 3, 7-8, 10-14, 19, 23-24 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (1999) in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. and Choo, Q.L. et al. (1991).

Applicant indicates that claims 3 and 19, from which all claims depend, have been amended to import limitations from claims 6 and 22, whereby the claim recites the limitation of SEQ ID NO:2. In fact, the claims do not include the limitation of SEQ ID NO:2, but rather "*at least 80% sequence identity* to the contiguous amino acid sequence of SEQ ID NO:2."

The claims are drawn to a method of detecting hepatitis C virus infection using a multiple epitope fusion antigen (MEFA) where the MEFA comprises at least one epitope in common with an NS3/4a antigen and either the antigen or the MEFA is used as the solid support. As mentioned above, Applicant has further amended the base claims 3 and 19 to obviate the prior rejection by adding the limitation wherein the NS3/4a antigen has an amino acid sequence with at least 80% sequence identity to the contiguous amino acid sequence of SEQ ID NO:2. Claims subsequent to claim 3 require that the MEFA and the antigen to possess at least one epitope from a specific region of the NS3/4a region. Claims 3, 6-16 and 33 are directed to a system whereby it is the "one or more NS3/4a antigens" that are bound to the solid support and the MEFA is subsequently added; a version of a double antigen bridge test. Claims 19 and 22-32 are

directed to a system whereby it is the MEFA bound to the solid support and it is the one or more antigens that are subsequently added; also a double antigen bridge.

Chien et al. (1999) Journal of Clinical Microbiology, vol. 37, No. 5; p. 1393-97 teach a method of detecting hepatitis C virus infection in a biological sample using a MEFA containing all of the major immunogenic epitopes of HCV where the MEFA comprises at least one epitope in common with the antigen used in the solid support. (See abstract) Chien et al. (1999) is discussed more fully in the previous action. It was pointed out that Chien et al. (1999) did not employ a double antigen bridge test. As indicated in the previous Office Action in regards to claims 9 and 25, Figure 1 of Chien et al. (1992) on page 10012 indicates that the C33C polypeptide which was part of Chien's C25 chimeric polypeptide is derived from the NS3 region. Also on page 10012 Chien indicates that "the C33C polypeptide . . . is derived from most of the NS3 region that appears to encode both a viral protease and a helicase." (See the last full line of col. 1) Thus, it teaches or suggests the region from 1193-1657 as found in claims 9 and 25. Chien does not provide the particular sequence of his antigen across the NS3/4a region.

Also as indicated in the previous action, U.S. Patent No. 6,306,579 B1 ('579) teaches a double antigen bridge test using HCV antigens from the NS3 region in immunological tests (See col. 4, lines 16-25). The '579 patent indicates that, when compared to other formats, a double antigen bridge results in both increased sensitivity (other immunoglobulin classes are recognized) and increased specificity (fewer unspecific reactions are seen).

Choo, Q.L. et al. (1991) teaches the amino acid sequence of the HCV polyprotein. Choo's sequence is 99.5% identical to Applicant's SEQ ID NO. 2. See also the sequence alignment printout included with the present Office Action.

One of ordinary skill in the art would have been motivated to combine the teachings of Chien with those of the '579 patent to create an immunological test for the detection of HCV-specific antibodies using a MEFA in a double antigen bridge format because the '579 patent et al indicates that the double antigen bridge format results in increased specificity and sensitivity. Moreover, at 99.5% identity, Choo's published sequence falls squarely within Applicant's parameters of 80% sequence identity to the contiguous amino acid sequence of SEQ ID NO:2. One of ordinary skill in the art would have expected to produce an immunological test for the detection of HCV-specific antibodies using MEFAs with enhanced sensitivity because Chien et al. teaches the efficacy of MEFAs in binding HCV-specific antibody while the '579 patent teaches the improved performance of the double antigen bridge format in the context of an immunological test for HCV-specific antibody to the NS3 region. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

3. Claims 9 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (1999) in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. and Choo, Q.L. et al. (1991) as applied to claims 3, 7-8, 10-14, 19, 23-24 and 26-30 above, and further in view of Chien et al. (1992).

Claims 9 and 25 indicate that the MEFA comprises amino acids 1193-1657 of the HCV sequence. This is the portion of NS3 that corresponds to the helicase region.

Figure 1 of Chien et al. (1992) on page 10012 indicates that the C33C polypeptide which was part of Chien's C25 chimeric polypeptide is derived from the NS3 region. Also on page 10012 Chien indicates that "[t]he C33C polypeptide ... is derived from most of the NS3 region that appears to encode both a viral protease and a helicase." (See the last full line of col. 1) It is not clear from the disclosure whether Chien included the entire helicase region in his MEFA, as currently claimed by applicant, but the statement certainly strongly suggests its inclusion.

One of ordinary skill in the art would have been motivated to include the helicase peptide in a MEFA containing epitopes directed against the NS3/4a region of the HCV polypeptide because Chien et al. showed the efficacy of helicase epitopes and indicated the importance of the inclusion of antigenic determinants from the helicase region. One of ordinary skill in the art would have expected to produce a MEFA capable of detecting antibody specific to the helicase region because Chien et al. teaches the efficacy of such an epitope in a MEFA. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

4. Claims 1-5, 7-8, 10-21, 23-24 and 26-32 were rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,428,792 B1 ('792) to Valenzuela in view of U.S. Patent No. 6,306,579 B1 ('579) to Seidel. Claims 15, 16, 31 and 32 were further rejected under 35 U.S.C. 103(a) over Valenzuela in view of Seidel as outlined on page

10 of the prior action. These rejections are withdrawn pursuant to Applicant's cancellation of claims 1, 2, 4, 5, 17, 18, 20 and 21 and Applicant's amendment of claims 3 and 19 adding the limitation directed at identity to SEQ ID NO:2.

5. Claims 3, 7-8, 10-14, 19, 23-24 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,428,792 to Valenzuela et al. in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. and Choo, Q.L. et al. (1991).

Valenzuela et al. (US Pat. No. 6,428,792 B1) teach a method of detecting hepatitis C virus infection in a biological sample using a MEFA containing all of the major immunogenic epitopes of HCV where the MEFA comprises at least one epitope in common with the antigen used in the solid support (See abstract) Valenzuela's MEFA-3, MEFA-5 and MEFA-6 chimeric polypeptides included epitopes from the NS3(protease)/NS4a(helicase) region (see fig. 1A-1C). Valenzuela employed a system whereby the MEFA was coated on the plates, test sample containing anti-HCV antibody was added, and then conjugated antibody was added to detect the anti-HCV antibody bound to the MEFA. Thus, Valenzuela et al did not employ a double antigen bridge test.

Seidel et al teach a double antigen bridge test using HCV antigens from the NS3 region in immunological tests (U.S. Pat. No. 6,306,579 B1). (See col. 4, lines 16-25). Seidel indicates that, when compared to other formats, a double antigen bridge results in both increased sensitivity (other immunoglobulin classes are recognized) and increased specificity (fewer unspecific reactions are seen).

Choo, Q.L. et al. (1991) teaches the amino acid sequence of the HCV polyprotein. Choo's sequence is 99.5% identical to Applicant's SEQ ID NO. 2. See also the sequence alignment printout included with the present Office Action.

One of ordinary skill in the art would have been motivated to combine the teachings of Valenzuela with those of Seidel to create an immunological test for the detection of HCV-specific antibodies using MEFA in a double antigen bridge format because Seidel et al indicates that the double antigen bridge format results in increased specificity and sensitivity. One of ordinary skill in the art would have expected to produce an immunological test for the detection of HCV-specific antibodies using MEFAs with enhanced sensitivity because Valenzuela et al. teaches the efficacy of MEFAs in binding HCV-specific antibody while Seidel teaches the improved performance of the double antigen bridge format in the context of an immunological test for HCV-specific antibody to the NS3 region. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

6. Claims 9 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,428,792 to Valenzuela et al. in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. and Choo, Q.L. et al. (1991) as applied to claims 3, 7-8, 10-14, 19, 23-24 and 26-30 above, and further in view of Chien et al. (1992).

Claims 9 and 25 indicate that the MEFA comprises amino acids 1193-1657 of the HCV sequence. This is the portion of NS3 that corresponds to the helicase region.

Figure 1 of Chien et al. (1992) on page 10012 indicates that the C33C polypeptide which was part of Chien's C25 chimeric polypeptide is derived from the NS3 region. Also on page 10012 Chien indicates that "[t]he C33C polypeptide ... is derived from most of the NS3 region that appears to encode both a viral protease and a helicase." (See the last full line of col. 1) It is not clear from the disclosure whether Chien included the entire helicase region in his MEFA, as currently claimed by applicant, but the statement certainly strongly suggests its inclusion.

One of ordinary skill in the art would have been motivated to include the helicase peptide in a MEFA containing epitopes directed against the NS3/4a region of the HCV polypeptide because Chien et al. showed the efficacy of helicase epitopes and indicated the importance of the inclusion of antigenic determinants from the helicase region. One of ordinary skill in the art would have expected to produce a MEFA capable of detecting antibody specific to the helicase region because Chien et al. teaches the efficacy of such an epitope in a MEFA. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

7. Claims 1-5, 7-14, 17-21 and 23-30 were rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (1992) in view of Seidel et al. These rejections are withdrawn pursuant to Applicant's cancellation of claims 1, 2, 4, 5, 17, 18, 20 and 21 and Applicant's amendment of claims 3 and 19 adding the limitation directed at identity to SEQ ID NO:2.

8. Claims 3, 7-14, 19 and 23-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (1992) in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. and Choo, Q.L. et al. (1991).

The claims are drawn to a method of detecting hepatitis C virus infection using a multiple epitope fusion antigen (MEFA) where the MEFA comprises at least one epitope in common with an antigen and either the antigen or the MEFA is used as the solid support. Claims subsequent to claim 1 require that the MEFA and the antigen to possess at least one epitope from the NS3/4a region or a specific region of the NS3/4a region.

Chien et al. (1992) Proc. Nat. Acad. Sci., vol. 89; pp. 10011-10015 teach an immunodominant chimeric polyprotein, which would also constitute a MEFA, using regions from NS3, NS4 and C of HCV to be used in assays formats such as ELISAs. The epitopes in one of the chimeric polyproteins, designated c25, is shown in fig. 1 on page 10012. The c25 polyprotein contained epitopes from the the NS3(protease)/NS4a(helicase) region. Chien et al did not employ a double antigen bridge test. Claims 9 and 25 indicate that the MEFA comprises amino acids 1193-1657 of the HCV sequence. This is the portion of NS3 that corresponds to the helicase region. Figure 1 of Chien et al. (1992) on page 10012 indicates that the C33C polypeptide which was part of Chien's C25 chimeric polypeptide is derived from the NS3 region. Also on page 10012 Chien indicates that "[t]he C33C polypeptide ... is derived from most of the NS3 region that appears to encode both a viral protease and a helicase." (See the last full line of col. 1) It is not clear from the disclosure whether

Chien included the entire helicase region in his MEFA, as currently claimed by applicant, but the statement certainly strongly suggests its inclusion.

Seidel et al teach a double antigen bridge test using HCV antigens from the NS3 region in immunological tests (U.S. Pat. No. 6,306,579 B1). (See col. 4, lines 16-25). Seidel indicates that, when compared to other formats, a double antigen bridge results in both increased sensitivity (other immunoglobulin classes are recognized) and increased specificity (fewer unspecific reactions are seen).

Choo, Q.L. et al. (1991) teaches the amino acid sequence of the HCV polyprotein. Choo's sequence is 99.5% identical to Applicant's SEQ ID NO. 2. See also the sequence alignment printout included with the present Office Action.

One of ordinary skill in the art would have been motivated to combine the teachings of Chien with those of Seidel to create an immunological test for the detection of HCV-specific antibodies using MEFA in a double antigen bridge format because Seidel et al indicates that the double antigen bridge format results in increased specificity and sensitivity. One of ordinary skill in the art would have expected to produce an immunological test for the detection of HCV-specific antibodies using MEFAs with enhanced sensitivity because Chien et al. teaches the efficacy of MEFAs in binding HCV-specific antibody while Seidel teaches the improved performance of the double antigen bridge format in the context of an immunological test for HCV-specific antibody to the NS3 region. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

9. The rejection of claims 6, 15, 16, 22, 31 and 32 under 35 U.S.C. 103(a) as being unpatentable over WO200196870-A2 to Chien et al. in view of U.S. Patent No. 6,306,579 B1 to Seidel et al. is withdrawn in view of Applicant's declaration regarding inventorship filed with the present response on November 18, 2004.

Double Patenting

The following obviousness-type double patenting rejections from the previous action is ***maintained***:

Claims 1-30 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,428,792 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application are broadly directed at methods of using MEFAs, while the claims of the patent are directed to broad product claims for MEFAs while disclosing the utility of such MEFAs in exactly the immunoassay format claimed in the methods of the present application. Furthermore, the MEFA claims of the prior patent read on the MEFAs disclosed in the methods of the present application. See for instance claims 1, 17.

The following obviousness-type double patenting rejections are made in the present Office Action:

Claims 3, 6-16, 19, and 22-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S.

Patent No. 6,632,601. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '601 patent claims a methods of detecting HCV using an immunoassay employing NS3/4a where the sequence of the NS3/4a is 100% identical to SEQ ID NO:2. See for instance claim 19.

Claims 3, 6-16, 19, and 22-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,797,809. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '809 patent claims a MEFA and teaches its use in immunoassays involving NS3/4a.

Claims 3, 6-16, 19, and 22-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,630,298. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '298 patent claims an immunoassay involving NS3/4a and MEFAs and methods of use therof. See for instance claim 9.

Claims 3, 6-16, 19, and 22-32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of copending Application No. 10/643,853. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications involve the use of MEFAs and NS3/4a in immunoassays.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 3, 6-16, 19, and 22-32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-49 of copending Application No. 10/174,652. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications involve the use of MEFAs and NS3/4a in immunoassays.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 3, 6-16, 19, and 22-32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-47 of copending Application No. 10/899,716. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications involve the use of MEFAs and NS3/4a in immunoassays.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

Claim 6, 15, 16, 22, 31 and 32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: Claims 6 and 22 specify that the Ns3/4a sequence is SEQ ID NO: 2. The sequence is free of the prior art. SEQ ID NO: 2 was created by a contiguous 2 amino

acid change whereby the residues CS or CA, as found in the "5-1-1" region of the HCV polyprotein, were substituted with the contiguous residues PI. (See page 36 of the specification) The closest prior art is Choo et al. discussed above and teaching an amino acid sequence 99.5% identical to Applicant's SEQ ID NO:2 and Chien et al. (1992) teaching the use of a fused, chimeric polyprotein (C25) composed of the NS3, NS4 and the C regions of HCV in an immunoassay. SEQ ID NO: 4 is taught in U.S. Patent Nos. 6,630,298 which is commonly assigned. A double patenting rejection has been made. SEQ ID NO: 6 is taught in U.S. Patent Nos. 6,632,601 which is commonly assigned. A double patenting rejection has been made. SEQ ID NO:4 or SEQ ID NO:6 with the limitations of the rejected base claims is otherwise free of the prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

M. M.

Michael M. McGaw

Sunday, January 23, 2005

James C. Housel 1/24/05

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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DR   InterPro; IPR002522; HCV_capsid.
DR   InterPro; IPR002521; HCV_core.
DR   InterPro; IPR002519; HCV_env.
DR   InterPro; IPR002531; HCV_NS1.
DR   InterPro; IPR002518; HCV_NS2.
DR   InterPro; IPR000745; HCV_NS4a.
DR   InterPro; IPR001490; HCV_NS4b.
DR   InterPro; IPR002868; HCV_NS5a.
DR   InterPro; IPR002166; HCV_RdRP.
DR   InterPro; IPR001650; Helicase_C.
DR   InterPro; IPR004109; Peptidase_C29.
DR   InterPro; IPR007095; RNA_pol_DS_PS.
DR   InterPro; IPR007094; RNA_pol_PSvir.
DR   Pfam; PF01543; HCV_capsid; 1.
DR   Pfam; PF01542; HCV_core; 1.
DR   Pfam; PF01539; HCV_env; 1.
DR   Pfam; PF01560; HCV_NS1; 1.
DR   Pfam; PF01538; HCV_NS2; 1.
DR   Pfam; PF02907; HCV_NS3; 1.
DR   Pfam; PF01006; HCV_NS4a; 1.
DR   Pfam; PF01001; HCV_NS4b; 1.
DR   Pfam; PF01506; HCV_NS5a; 1.
DR   Pfam; PF00271; helicase_C; 1.
DR   Pfam; PF00998; Viral_RdRP; 1.
DR   ProDom; PD186062; HCV_NS1; 1.
DR   SMART; SM00487; DEXDc; 1.
KW   Polyprotein; Glycoprotein; Transferase; RNA-directed RNA polymerase;
KW   Core protein; Coat protein; Envelope protein; Helicase; ATP-binding;
KW   Transmembrane; Nonstructural protein; Hydrolase; Serine protease;
KW   3D-structure.
FT   INIT_MET      1      1       REMOVED FROM CAPSID PROTEIN C BY THE
FT                                CELLULAR AMINOPEPTIDASE.
FT   CHAIN         1    115       CAPSID PROTEIN C (POTENTIAL).
FT   CHAIN       116    191       MATRIX PROTEIN (POTENTIAL).
FT   CHAIN       192    383       MAJOR ENVELOPE PROTEIN E (POTENTIAL).
FT   CHAIN       384    729       NONSTRUCTURAL PROTEIN NS1/E2 (POTENTIAL).
FT   CHAIN       730   1006       NONSTRUCTURAL PROTEIN NS2 (POTENTIAL).
FT   CHAIN      1007   1615       PROTEASE/HELICASE NS3 (POTENTIAL).
FT   CHAIN      1616   1862       NONSTRUCTURAL PROTEIN NS4A (POTENTIAL).
FT   CHAIN      1863   2013       NONSTRUCTURAL PROTEIN NS4B (POTENTIAL).
FT   CHAIN      2014   3011       RNA-DIRECTED RNA POLYMERASE (POTENTIAL).
FT   TRANSMEM    347    369       POTENTIAL.
FT   ACT_SITE   1083   1083       CHARGE RELAY SYSTEM (BY SIMILARITY).
FT   ACT_SITE   1107   1107       CHARGE RELAY SYSTEM (BY SIMILARITY).
FT   ACT_SITE   1165   1165       CHARGE RELAY SYSTEM (BY SIMILARITY).
FT   NP_BIND    1230   1237       ATP (POTENTIAL).
FT   SITE       1316   1319       DECH BOX.
FT   CARBOHYD    196    196       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    209    209       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    234    234       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    305    305       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    417    417       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    423    423       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    430    430       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    448    448       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    476    476       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    532    532       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    540    540       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    556    556       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    576    576       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    623    623       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD    645    645       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2041   2041       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2077   2077       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2240   2240       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2364   2364       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   CARBOHYD   2789   2789       N-LINKED (GLCNAC. . .) (POTENTIAL).
SQ   SEQUENCE   3011 AA;  327197 MW;  65F8C9447FCE5AF9 CRC64;

  Query Match             99.5%;  Score 3602;  DB 1;  Length 3011;
  Best Local Similarity   99.6%;  Pred. No. 2.7e-248;
  Matches  683;  Conservative    1;  Mismatches    2;  Indels    0;  Gaps    0;

Qy          1 MAPITAYAQQTRGLLGCIITSLTGRDKNQVEGEVQIVSTAAQTFLATCINGVCWTVYHGA 60
              :|||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1026 LAPITAYAQQTRGLLGCIITSLTGRDKNQVEGEVQIVSTAAQTFLATCINGVCWTVYHGA 1085

Qy         61 GTRTIASPKGPVIQMYTNVDQDLVGWPAPQGSRSLTPCTCGSSDLYLVTRHADVIPVRRR 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1086 GTRTIASPKGPVIQMYTNVDQDLVGWPAPQGSRSLTPCTCGSSDLYLVTRHADVIPVRRR 1145

Qy        121 GDSRGSLLSPRPISYLKGSSGGPLLCPAGHAVGIFRAAVCTRGVAKAVDFIPVENLETTM 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1146 GDSRGSLLSPRPISYLKGSSGGPLLCPAGHAVGIFRAAVCTRGVAKAVDFIPVENLETTM 1205

Qy        181 RSPVFTDNSSPPVVPQSFQVAHLHAPTGSGKSTKVPAAYAAQGYKVLVLNPSVAATLGFG 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1206 RSPVFTDNSSPPVVPQSFQVAHLHAPTGSGKSTKVPAAYAAQGYKVLVLNPSVAATLGFG 1265

Qy        241 AYMSKAHGIDPNIRTGVRTITTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATS 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1266 AYMSKAHGIDPNIRTGVRTITTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATS 1325

Qy        301 ILGIGTVLDQAETAGARLVVLATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVI 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1326 ILGIGTVLDQAETAGARLVVLATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVI 1385

Qy        361 KGGRHLIFCHSKKKCDELAAKLVALGINAVAYYRGLDVSVIPPIGDVVVVATDALMTGYT 420
              |||||||||||||||||||||||||||||||||||||||||  ||||||||||||||||
Db       1386 KGGRHLIFCHSKKKCDELAAKLVALGINAVAYYRGLDVSVIPTSGDVVVVATDALMTGYT 1445

Qy        421 GDFDSVIDCNTCVTQTVDFSLDPTFTIETITLPQDAVSRTQRRGRTGRGKPGIYRFVAPG 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1446 GDFDSVIDCNTCVTQTVDFSLDPTFTIETITLPQDAVSRTQRRGRTGRGKPGIYRFVAPG 1505

Qy        481 ERPSGMFDSSVLCECYDAGCAWYELTPAETTVRLRAYMNTPGLPVCQDHLEFWEGVFTGL 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1506 ERPSGMFDSSVLCECYDAGCAWYELTPAETTVRLRAYMNTPGLPVCQDHLEFWEGVFTGL 1565

Qy        541 THIDAHFLSQTKQSGENLPYLVAYQATVCARAQAPPPSWDQMWKCLIRLKPTLHGPTPLL 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1566 THIDAHFLSQTKQSGENLPYLVAYQATVCARAQAPPPSWDQMWKCLIRLKPTLHGPTPLL 1625

Qy        601 YRLGAVQNEITLTHPVTKYIMTCMSADLEVVTSTWVLVGGVLAALAAYCLSTGCVVIVGR 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1626 YRLGAVQNEITLTHPVTKYIMTCMSADLEVVTSTWVLVGGVLAALAAYCLSTGCVVIVGR 1685

Qy        661 VVLSGKPAIIPDREVLYREFDEMEEC 686
              |||||||||||||||||||||||||
Db       1686 VVLSGKPAIIPDREVLYREFDEMEEC 1711


RESULT 2
POLG_HCVH
ID   POLG_HCVH      STANDARD;      PRT;  3011 AA.
AC   P27958;
DT   01-AUG-1992 (Rel. 23, Created)
DT   01-AUG-1992 (Rel. 23, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Genome polyprotein [Contains: Capsid protein C (Core protein) (P22);
DE   Envelope glycoprotein E1 (GP32) (GP35); Envelope glycoprotein E2
DE   (GP68) (GP70) (NS1); Protein P7; Nonstructural protein NS2 (P21)
DE   (EC 3.4.99.-); Protease/helicase NS3 (P70) (Hepacivirin)
DE   (EC 3.4.21.98); Nonstructural protein NS4A (P4); Nonstructural protein
DE   NS4B (P27); Nonstructural protein NS5A (P56); Nonstructural protein
DE   NS5B (P66) (P70) (RNA-directed RNA polymerase) (EC 2.7.7.48)].
OS   Hepatitis C virus (isolate H) (HCV).
OC   Viruses; ssRNA positive-strand viruses, no DNA stage; Flaviviridae;
OC   Hepacivirus.
OX   NCBI_TaxID=11108;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=92052256; PubMed=1658800;
RA   Inchauspe G., Zebedee S., Lee D.H.H., Sugitani M., Nasoff M.,
RA   Prince A.M.;
RT   "Genomic structure of the human prototype strain H of hepatitis C
```

Sequence Alignment

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: June 21, 2004, 10:18:59 ; Search time 9.18516 Seconds
(without alignments)
3888.897 Million cell updates/sec

Title: US-10-658-782-2
Perfect score: 3619
Sequence: 1 MAPITAYAQQTRGLLGCIIT.....PAIIPDREVLYREFDEMEEC 686

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

SEQ ID NO: 2

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_42:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	3602	99.5	3011	1	POLG_HCV1	P26664 h genome po
2	3513	97.1	3011	1	POLG_HCVH	P27958 h genome po
3	3426	94.7	3010	1	POLG_HCVBK	P26663 h genome po
4	3417	94.4	3010	1	POLG_HCVJT	Q00269 h genome po
5	3408	94.2	3010	1	POLG_HCVJA	P26662 h genome po
6	3402	94.0	3010	1	POLG_HCVTW	P29846 h genome po
7	2989	82.6	3033	1	POLG_HCVJ6	P26660 h genome po
8	2979	82.3	3033	1	POLG_HCVJ8	P26661 h genome po
9	273	7.5	3898	1	POLG_HCVA	P19712 hog cholera
10	273	7.5	3898	1	POLG_HCVB	P21530 hog cholera
11	268.5	7.4	3988	1	POLG_BVDVN	P19711 bovine vira
12	267.5	7.4	3898	1	POLG_BVDVS	Q01499 bovine vira
13	227.5	6.3	3341	1	POLG_MCFA	P33515 m genome po
14	206	5.7	3140	1	POLG_PPVSK	Q84934 p genome po
15	202	5.6	3125	1	POLG_PPVNA	P17766 p genome po
16	201	5.6	3140	1	POLG_PPVRA	P17767 p genome po
17	201	5.6	3141	1	POLG_PPVD	P13529 p genome po
18	200	5.5	3023	1	POLG_TVMV	P09814 t genome po
19	199.5	5.5	3083	1	POLG_ZYMVR	Q89330 z genome po
20	199.5	5.5	3255	1	POLG_LMV0	P31999 l genome po
21	199	5.5	3054	1	POLG_TEV	P04517 t genome po
22	196	5.4	3432	1	POLG_JAEVJ	P32886 j genome po
23	195	5.4	3432	1	POLG_JAEV1	P27395 j genome po
24	194	5.4	3391	1	POLG_DEN26	P29990 d genome po
25	194	5.4	3432	1	POLG_JAEV5	P19110 j genome po
26	193.5	5.3	3411	1	POLG_YEFV1	P03314 y genome po
27	193.5	5.3	3411	1	POLG_YEFV2	P19901 y genome po
28	192	5.3	3163	1	POLG_TUMVQ	Q02597 t genome po
29	192	5.3	3164	1	POLG_TUMVJ	P89509 t genome po
30	191.5	5.3	3255	1	POLG_LMVE	P89876 l genome po
31	189	5.2	3066	1	POLG_SBMVN	P21231 s genome po
32	187	5.2	3391	1	POLG_DEN27	P29991 d genome po
33	187	5.2	3391	1	POLG_DEN2N	P14340 d genome po
34	185	5.1	3206	1	POLG_PSBMV	P29152 p genome po
35	185	5.1	3391	1	POLG_DEN2J	P07564 d genome po
36	182.5	5.0	3080	1	POLG_ZYMVC	P18479 z genome po
37	182.5	5.0	3390	1	POLG_DEN3	P27915 d genome po
38	182	5.0	3396	1	POLG_DEN1S	P33478 d genome po
39	182	5.0	3433	1	POLG_KUNJM	P14335 k genome po
40	181	5.0	1683	1	POLG_DEN2T	P27914 dengue viru
41	181	5.0	3066	1	POLG_SBMVG	Q90069 s genome po
42	181	5.0	3388	1	POLG_DEN2P	P12823 d genome po
43	181	5.0	3430	1	POLG_WNV	P06935 w genome po
44	180.5	5.0	3061	1	POLG_PVYHU	Q02963 p genome po
45	180.5	5.0	3083	1	POLG_ZYMVS	O36979 z genome po

ALIGNMENTS

RESULT 1
POLG_HCV1
ID POLG_HCV1 STANDARD; PRT; 3011 AA.
AC P26664;
DT 01-AUG-1992 (Rel. 23, Created)
DT 01-AUG-1992 (Rel. 23, Last sequence update)
DT 10-OCT-2003 (Rel. 42, Last annotation update)
DE Genome polyprotein [Contains: Capsid protein C (Core protein) (P22);
DE Envelope glycoprotein E1 (GP32) (GP35); Envelope glycoprotein E2
DE (GP68) (GP70) (NS1); Protein P7; Nonstructural protein NS2 (P21)
DE (EC 3.4.22.-); Protease/helicase NS3 (P70) (Hepacivirin)
DE (EC 3.4.21.98); Nonstructural protein NS4A (P4); Nonstructural protein
DE NS4B (P27); Nonstructural protein NS5A (P56); Nonstructural protein
DE NS5B (P66) (P70) (RNA-directed RNA polymerase) (EC 2.7.7.48)].
OS Hepatitis C virus (isolate 1) (HCV).
OC Viruses; ssRNA positive-strand viruses, no DNA stage; Flaviviridae;
OC Hepacivirus.
OX NCBI_TaxID=11104;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=91172826; PubMed=1848704;
RA Choo Q.-L., Richman K.H., Han J.H., Berger K., Lee C., Dong C.,
RA Gallegos C., Coit D., Medina-Selby A., Barr P.J., Weiner A.J.,
RA Bradley D.W., Kuo G., Houghton M.;
RT "Genetic organization and diversity of the hepatitis C virus.";
RL Proc. Natl. Acad. Sci. U.S.A. 88:2451-2455(1991).
CC -!- FUNCTION: The small proteins NS2A, NS2B, NS4A and NS4B are
CC hydrophobic, suggesting a possible membrane-related function. NS3
CC and NS5 may play a role in the viral RNA replication.
CC -!- CATALYTIC ACTIVITY: Hydrolysis of four peptide bonds in the viral
CC precursor polyprotein, commonly with Asp or Glu in the P6
CC position, Cys or Thr in P1 and Ser or Ala in P1'.
CC -!- CATALYTIC ACTIVITY: N nucleoside triphosphate = N diphosphate +
CC {RNA}(N).
CC -!- SUBUNIT: The virion of this virus is a nucleocapsid covered by a
CC lipoprotein envelope. The envelope consists of two proteins:
CC protein M and glycoprotein E. The nucleocapsid is a complex of
CC protein C and mRNA.
CC -!- SIMILARITY: THE PROTEASE BELONGS TO PEPTIDASE FAMILY S29.
CC ---

CC ---
DR EMBL; M62321; AAA45676.1; -.
DR PIR; A39166; GNWVC3.
DR PDB; 1A1V; 16-FEB-99.
DR PDB; 1HEI; 25-NOV-98.
DR MEROPS; S29.001; -.
DR MEROPS; U39.001; -.
DR InterPro; IPR009003; Cys_Ser_trypsin.
DR InterPro; IPR001410; DEAD.